

The Crystal Structure of the SIV gp41 Ectodomain at 1.47 Å Resolution

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Cell membrane fusion by human (HIV) and simian (SIV) immunodeficiency viruses is mediated by the envelope glycoproteins gp120 and gp41. Although the precise mechanism of the fusion process is unknown, the ectodomain of gp41 is thought to undergo dramatic rearrangement from its prefusogenic state. To elucidate this process further, the crystal structure of the SIV gp41 ectodomain (residues 27-149) was determined at 1.47 Å resolution and is reported herein. It is the most accurate and complete structure of a retroviral gp41 ectodomain determined to date. The rod-like trimeric structure of SIV gp41 comprises three parallel N-terminal alpha-helices assembled as a coiled coil in the center with three antiparallel C-terminal alpha-helices packed on the outside connected by highly flexible loops. Portions of the loops in all three monomers are crystallographically disordered and could not be accurately modeled. The core of the structure is similar (but not identical) to those of smaller HIV/SIV gp41 segments previously determined by X-ray crystallography with root mean square deviations in main chain atoms of less than 1.0 Å. The crystal structure differs more substantially from the reported NMR solution structure of the identical SIV construct. The mechanisms of viral fusion and the inhibition by peptides are discussed in the context of the three-dimensional structure.